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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Tai-Shun Lin and William H. Prusoff
Serial No. : 06/942,666
Filed : December 17, 1986
For : USE OF 3'-DEOXYTHYMIDIN-2'-ENE (3' DEOXY-
2',3'-DIDEHYDROTHYMIDINE) IN TREATING
PATIENTS INFECTED WITH RETROVIRUSES
Art Unit : 123
Examiner : J. Tou

Hon. Commissioner of Patents
& Trademarks
Washington, D.C. 20231

Sir:

DECLARATION UNDER RULE 132 OF DR. WILLIAM H. PRUSOFF

I, William H. Prusoff, declare and state that

1. I am a Professor of Pharmacology at Yale University.

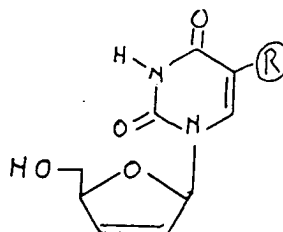
2. Appended hereto and made a part hereof is my curriculum vitae which gives further details of my background and experience. Based on such background and experience, I believe I am an expert in the field of the above-identified patent application.

3. I am an applicant of the above-identified patent application.

4. Under my supervision a side-by-side in vitro comparison was carried out of a compound for use in the above-identified invention, namely,
3'-deoxythymidin-2'-ene(3'-deoxy- 2',3'-didehydrothymidine; d4T) with a comparable compound wherein the methyl moiety (C1) was replaced with the next higher alkyl, an ethyl moiety (C2) with respect to antiviral activity against HIV-1 (the AIDS virus) in H9 cells.

The results given hereinbelow clearly indicated potent activity when R1 is C1 (that is a methyl group) and no activity when R1 is C2 (that is an ethyl group).

Hence the most closely related compound has no activity, and therefore, it is not obvious from Verheyden et al (wherein R1 is a C3 to C7 alkyl) that the compound for use in the invention (when R1 is a C1 alkyl) would have such potent antiviral activity against the AIDS virus (HIV-1).



3'-Deoxythymidin-2'-ene (5-methyl-2',3'-dideoxyuridin-2'-ene; d4T)



5-Ethyl-2',3'-dideoxyuridin-2'-ene

Inhibition of HIV-1

<u>(R)</u>	<u>Concentration (μM)</u>	<u>% Inhibition</u>
-CH ₃	5	70
	10	77
	50	97
-C ₂ H ₅	5	0
	10	0
	50	0

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Date

4/28/88

William H. Prusoff
William H. Prusoff

CURRICULUM VITAE

William Herman Prusoff

Born: June 25, 1920, New York City

Marriage: June 19, 1948, to Brigitte Auerbach

Education:

B.S. University of Miami, Coral Gables, Florida 1941
M.S. Columbia University, New York City 1947
Ph.D. Columbia University, New York City 1949

Career:

1941-43 Ordinance Inspector, Milan, Tenn. (War Dept.)
1943-44 Assistant Chemist, Miami Beach, Florida (War Dept.)
1944-49 Research Assistant, Columbia University
1949-53 Research Associate and Instructor of Pharmacology,
Western Reserve University School of Medicine.
Department of Pharmacology, Yale University School of
Medicine
1954-59 Assistant Professor, Yale University
1959-66 Associate Professor, Yale University
1959-60 Oxford University, Oxford, England, Special
traineeship award from National Institute of
Neurological Diseases and Blindness.
1966- Professor, Department of Pharmacology, Yale
University School of Medicine
1968-69 Acting Chairman

Membership in the following organizations:

American Association for Cancer Research
American Society for Pharmacology and Experimental Therapeutics
American Society of Biological Chemists
American Chemical Society
Sigma Xi
American Society for Microbiology
American Society for Virology
Inter-American Society for Chemotherapy
Society of Chinese Bioscientists in America

Other Professional Responsibilities:

1966-71 Member of American Cancer Society Research Advisory Committee
1969-73 Member of Pharmacology B Study Section of NIH
1969-80 Member of the Editorial Board of the Journal Chemico-
Biological Interactions
1978-80 Associate Editor of The Yale Journal of Biology and Medicine
1976- Member of the Editorial Board of "Pharmacology and
Therapeutics"
1980- Member of the Editorial Board of "Antiviral Research"
1982-86 Member of American Cancer Society Advisory Committee on
Personnel for Research

Honors

Recipient of the 1982 ASPET Award in Experimental Therapeutics

Recipient of the 1988 International Society for Antiviral Research award
for continuing contributions in antiviral research.

Publications

215 full papers